REMARKS

STATUS OF THE CLAIMS:

Claims 1 to 20, 26 to 30, 32, 36, 37, and 38 to 40 are cancelled.

Claims 21 and 31 were amended.

Claims 21 to 25, 31, 33 to 35, and 41 to 44 are pending.

Claim 21 was amended to change "(g)" to "(c)" in order to place this sub-part into its proper context in light of Applicants August 18th, 2003 amendments to this claim in which sub-parts "(c)", "(d)", "(e)", and "(f)" were deleted. Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim. Applicants reserve the right to prosecute Claim 21 as originally presented in related applications. Applicants right to equivalents of Claim 21 is reserved. No new matter has been added.

Claim 21 was further amended to delete the "(antisense)" limitation of Claim 21(g), which is now Claim 21(c) in consideration of the amendment provided *supra*. Applicants believe this amendment clarifies the intended subject matter for this claim and places it in better form for allowance. No new matter has been added.

Claim 31 was amended to change "(g)" to "(c)" in order to place this sub-part into its proper context in light of the Claim 21 amendment provided *supra,* in addition to ensuring this claim maintains proper dependency. Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim. Applicants reserve the right to prosecute Claim 31 as originally presented in related applications. Applicants right to equivalents of Claim 31 is reserved. No new matter has been added.

I. Rejections under 35 U.S.C. § 101

a. The Examiner has rejected Claims 21 to 25, 31, 33 to 37, and 41 to 44 under 35 U.S.C. § 101, for failure to demonstrate a specific and substantial asserted utility or a well-established utility. More particularly, the Examiner alleges that "[t]he specification fails to provide sufficient objective evidence of any activity for encoded protein. Applicant only states that said protein shows 47 % identity to human SLAP and 58 % identity to the mouse SLAP proteins (see Table 4 and page 61, lines 22-30 in particular). The specification disclosed that based on sequence homology to related molecules, said protein may be a novel human SLAP-2 protein. The specification also disclosed that said hSLAP-2 nucleic acid sequence and related protein can be used for diagnosing, treating or preventing disorders or diseases associated with aberrant or uncontrolled cellular signal transduction or with hyperactive cell, or may play a role in one or more aspects of regulating the immune system and tumor cell biology (see page 20, lines 5-20 and page 41, lines 22-30 in particular). No well-established utility for a human SLAP-2 protein is indicated".

Applicants disagree and point out that the Examiner's position on utility is not in accordance with US patent law, nor is the Examiner's position in accordance with the guidance provided by the U.S.P.T.O in the Revised Interim Utility Guidelines. As Applicants pointed out in their August 18th, 2003 Reply, U.S. patent law does not require that a specification actually demonstrate use of a claimed invention. Rather, it is established law that a disclosure is enabling so long as it contains information which would lead one of ordinary skill in the art to *reasonably believe* the claimed invention has utility. *In re Barr*, 170 U.S.P.Q. 330 (C.C.P.A. 1971). In the absence of evidence or apparent reason why the claimed polynucleotides do not possess the disclosed utility, the allegation of utility in the specification *must* be accepted as correct. *Ex parte Krenzer*, 199 U.S.P.Q. 227 (Pat. Off. Bd. App. 1978).

Applicants pointed out to the Examiner in Applicants August 18th, 2003 Reply the objective evidence disclosed in Applicants specification that support Applicants assertion that one skilled in the art would reasonably believe that hSLAP-2 is a new member of the SLAP family of adapter proteins based not only on the high percent identity shared between the human and mouse SLAP proteins, but also the presence of the conserved SH2/SH3 domains which are essential to adaptor protein function (see pages 10 to 14 of Applicants August 18th, 2003 Reply). Applicants believe this information is sufficient to establish that a skilled artisan would reasonably believe that hSLAP-2 is a new member of the SLAP family of adapter proteins.

Applicants also pointed out to the Examiner further objective evidence disclosed in Applicants specification supporting Applicants assertions that one skilled in the art would reasonably believe that hSLAP-2 is a new member of the SLAP family of adapter proteins based upon the high percent identity between the hSLAP-2 SH2 and SH2/SH3 domains to the SH2 and SH2/SH3 domains of Lyn and Hck tyrosine kinases from the Src-family. Applicants pointed out the significance of this result by referring the Examiner to the teachings of Kelly et al., Curr. Opin. Immunol., 12:267-275 (2000); Tomlinson et al., Immunol. Today 21:584-591 (2000); Myung et al., Curr. Opin. Immunol., 12:256-266 (2000); and Kurosaki, T. et al., Ann. Rev. Immunol., 17:555-592 (1999), which, in summary, provide the basis for the appreciation in the art that distinct signaling cascades required for lymphocyte activation depend upon the involvement of specific adaptor proteins.

Applicants also pointed out to the Examiner that the hSLAP-2, like SLAP, has a restricted expression pattern being primarily expressed in "immune system cells includ[ed]ing peripheral blood lymphocytes, Jurkat T-cells and bone-marrow cells". In consideration of the totality of evidence provided in Applicants specification, Applicants asserted that one skilled in the art would reasonably believe that hSLAP-2 is a new member of the SLAP family of adapter proteins.

After establishing the strong supporting evidence that hSLAP-2 is a new member of the SLAP family of adapter proteins, Applicants also pointed out the utilities for hSLAP-2 as disclosed in Applicants specification. Specifically, Applicants pointed out that the specification teaches that the hSLAP-2 polypeptide is an adaptor protein which functions "in the receptor-ligand signal transduction pathway in cells of the hematopoietic lineage" (see paragraph 54 of specification). More particularly, Applicants specification teaches that hSLAP-2 is a "negative regulator[s] of intracellular signal transduction in several cell types, including T-cells" (see paragraph 76). Applicants specification also teaches that hSLAP-2 is useful for "the diagnosis, screening, monitoring, therapy, and prevention of immune system related conditions or diseases, particularly those involving T-cell and B-cell neoplasms; inflammation disorders, diseases and conditions, rheumatoid arthritis, osteoarthritis, psoriasis, rhinitis, inflammatory bowel disease (Crohn's and ulcerative colitis), allergies, particularly those involving hyperactivity of B-cells and T-cells, or other immune cells, such as mast cells or eosinophils; autoimmune diseases such as systemic lupus erythematosus and multiple sclerosis; pulmonary diseases including asthma, acute respiratory distress syndrome, and chronic obstructive pulmonary disorder; tissue/ organ rejection; and cancer" (see paragraph 12).

Applicants also referred the Examiner to three post-filing publications from three independent groups, namely Pandey et al, Holland et al, and Loreto et al, that completely corroborated the teachings of Applicants specification relating to the description of hSLAP-2 as a new member of the SLAP family of adaptor proteins, in addition to its utility as a negative modulator of T-cell activation. Specifically, Pandey et al, Holland et al, and Loreto et al identified a protein identical to hSLAP-2, recognized hSLAP-2 as representing a new member of the SLAP family of adapter proteins using the same criteria utilized by Applicants (e.g., percent homology, shared structural features, etc.), and established experimentally that hSLAP-2 functions as originally conceived in Applicants specification (e.g., as a negative modulator of T-cell activation).

Applicants also pointed out to the Examiner that the instant specification teaches that hSLAP-2 is capable of binding to ZAP-70 and that one skilled in the art would appreciate that any molecule that binds to ZAP-70 would be expected to affect T-cell receptor signaling and thus would be useful as a target for therapeutic intervention for disorders affecting T-cell antigen receptor signaling, such as T-cell tumors, lymphomas, leukemias, thymomas, and autoimmune disorders, among others (see paragraph 9). This rational is supported by the teachings of Chen et al., Cell 71:649-662 (1992); Zhang et al., Cell 92:83-92 (1998); Chan et al., EMBO J. 14:2499-2508 (1995); Williams et al., J. Biol. Chem. 271:19641-19644 (1996); and Williams et al., Mol. Cell. Biol., 18:1388-1399 (1998); and is based upon the fact that ZAP-70 links the activated T-cell receptor to downstream signaling events that ultimately leads to the transcription of genes such as IL-2, which is a hallmark of T-cell activation.

Both Pandey et al and Loreto et al demonstrate experimentally that hSLAP-2 is capable of binding to ZAP-70 and teach that this is the mechanism by which hSLAP-2 negatively affects T-cell receptor activation. Applicants believe this information alone demonstrates that hSLAP-2 has a well-established utility and was specifically taught by the teachings of Applicants specification.

In consideration of the fact that 1.) the requisite teachings demonstrating that hSLAP-2 is a new member of the SLAP family of adaptor proteins is found within Applicants specification as originally filed; 2.) the fact that the description of the anticipated function and utility of hSLAP-2 is found within Applicants specification as originally filed; and 3.) the fact that three independent groups, namely Pandey et al, Holland et al, and Loreto et al, published papers confirming that hSLAP-2 is a new member of the SLAP family of adaptor proteins, has the same physiological function as taught in Applicants specification as originally filed, and functions via the same mechanism as taught in Applicants specification as originally filed; supports Applicants arguments

that the Examiners maintenance of the utility rejection for the pending claims is erroneous and should be withdrawn.

Moreover, Applicants pointed out to the Examiner that the asserted utilities are specific, substantial and that the skilled artisan would credibly believe that hSLAP-2 has the asserted utilities as a consequence of the strong supporting evidence that hSLAP-2 is a new member of the SLAP family of adapter proteins, and that it functions as a negative regulator of T-cell receptor activation.

Specifically, Applicants pointed out to the Examiner that the utility of hSLAP-2 is "specific" since modulation of T-cell receptor activation is specific to methods of treating and/or diagnosing immune disorders specific to aberrant T-cell receptor activity since "unregulated activation of the T-cell receptor (TCR) can lead to aberrant T-cell growth, resulting in, for example, T-cell tumors, lymphomas, leukemias and thymomas" (see Applicants August 18th, 2003 Reply, page 12). Since one of the utilities of hSLAP-2 relates to methods of treating aberrant T-cell receptor disorders, the Examiner is reminded that asserting the utility rejection on this basis is not in accordance with the guidance provided in the Revised Interim Utility Guidelines since "most diseases or conditions can be treated, rejections under 35 U.S.C 101 for treatment claims should rarely be made". Applicants request that the utility rejection be withdrawn in acknowledgement of this guidance.

Applicants also pointed out that the utility of hSLAP-2 represents a "substantial" utility and does not constitute a throw-away utility since its use in treating and/or diagnosing immune disorders specific to aberrant T-cell receptor activity represents a "real world" context of use. Since such a method of treatment necessarily encompasses specific diseases or disorders exemplified in Applicants specification, including for example, T-cell tumors, lymphomas, leukemias and thymomas, among others, Applicants point out that such a utility represents a "substantial" utility in accordance with the Revised Interim Utility Guidelines. The Guidelines that a method of treating a disorder represents a substantial utility unless the method does not specify the disease or condition to be treated. However, since Applicants specification describes specific diseases or disorders that hSLAP-2 would be useful in treating, the "substantial utility" criterion has been met. Applicants request that the utility rejection be withdrawn in acknowledgement of this guidance.

Applicants also pointed out that the utility of hSLAP-2 is "credible" since one skilled in the art would clearly appreciate that hSLAP-2 is a new member of the SLAP family of adaptor proteins and would be expected to have the asserted utilities based upon the teachings of Applicants specification. The issue of whether such asserted utitilties are "credible" is moot in consideration of the independent corroborating support provided by Pandey et al, Holland et al, and Loreto et al.

Applicants again point the Examiner to the guidance provided by the Revised Interim Utility Guidelines which state that an "assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion". Since the asserted utilities were independently corroborated by three separate post-filing publications, Applicants adamantly assert that the "logic underlying the assertion" is clearly not flawed, nor are the facts flawed, since each of these publications support the teachings of Applicants application as originally filed relative to the hSLAP-2 representing a new member of the SLAP family of adaptors proteins, in addition to its role as a negative regulator of T-cell receptor activation. Applicants request that the utility rejection be withdrawn in acknowledgement of this guidance.

The Examiner has consistently alleged that the utility of a protein cannot be demonstrated by showing that a protein is homologous to another protein that has a well-known utility. Applicants point out that this argument is clearly erroneous in consideration of the fact that Applicants correctly identified the family to which hSLAP-2 belongs, correctly identified the physiological function of the hSLAP-2 protein, and correctly identified the mechanism by which hSLAP-2 mediates its function, as taught by Applicants specification as originally filed. Moreover, the fact that Pandey et al, Holland et al, and Loreto et al all ascribe the same family and functional assignments to hSLAP-2 using the same homology criteria as Applicants also clearly demonstrates that this type of association is well-established and commonly accepted in the art. In consideration of the latter, Applicants request that the Examiner concede the same and to introduce corrective statements into the record. The Examiners utility rejection as it relates to homology determinations is moot and is no longer applicable to the pending claims.

The Examiner has also consistently alleged that "the specification does not disclose any disease or conditions known to be associated with the hSLAP polypeptide, encoded by SEQ ID NO:2, or any conditions associated with altered levels (increase or decrease) of said polypeptide. Since any protein may potentially be used as a treatment agent, this utility would not be considered to be specific. Since no particular disease or condition is disclosed, the artisan would have been required to perform additional experimentation to identify and/or reasonably confirm the asserted use of hSLAP polypeptide as a treatment agent and therefore, this utility would not be considered to be substantial."

Applicants point out that the Examiners utility rejection based upon a failure to disclose any disease or condition known to be associated with hSLAP-2 goes against the tenets of U.S. patent

law, judicial precedent, as well as the U.S.P.T.O own guidance provided in the Revised Utility Examination Guidelines. The Examiners statement directly implies that there is no other means of meeting the utility requirement other than associating polynucleotides and polypeptides to a disease or disorder. Such a requirement is very limiting since only a small percentage of the known polynucleotides and polypeptides would ever be expected to be associated with a disease or disorder, and yet such polynucleotides and polypeptides would be expected to be useful in other applications. For example, a polypeptide may be useful for catalyzing a chemical reaction that is critical in the synthesis of a manufactured molecule. Such a use is clearly useful and is not associated with a disease or disorder. Another example may be the use of a polypeptide as a biomarker as a pharmakinetic indicator to assess the systemic level of a drug post administration. Again such a use is clearly useful and is associated with a disease or disorder. The utility guidelines only require that an asserted utility represent a specific, substantial, and credible or well-established utility and does not restrict the uses that would constitute such an acceptable utility, nor do the guidelines so limit the acceptable uses to only those applications specific to diseases or disorders. Applicants request that the utility rejection be withdrawn on these grounds and that the Examiner adhere to the guidance provided in the Revised Utility Examination Guidelines.

Nonetheless, as Applicants pointed out in the August 18th, 2003 Reply, hSLAP-2 has been associated to specific diseases or disorders based upon its negative modulation of T-cell receptor activation. As Applicants have pointed out *supra,* a number of diseases and disorders are associated with aberrant T-cell receptor activation including for example "T-cell tumors, lymphomas, leukemias, thymomas, and autoimmune disorders". Each of these diseases and disorders is specifically taught in Applicants specification as originally filed. Applicants assert that since one skilled in the art would readily appreciate that modulation of T-cell receptor activation would be useful for the treatment of these disorders, hSLAP-2 has a specific, substantial, credible, and well-established utility.

The Examiner has also maintained that the utility rejection was based upon the failure of Applicants specification to "disclose sufficient properties of SH2/SH3 domain-containing protein hSLAP-2 of SEQ ID NO:2 to support an inference of utility". As Applicants have noted above, the Examiners position is unfounded in consideration of the corroborative support provided in the post-filing publications of Pandey et al, Holland et al, and Loreto et al. Applicants adamantly assert that the independent confirmation by Pandey et al, Holland et al, and Loreto et al that hSLAP-2 is indeed a new member of the SLAP family of adaptor proteins, in addition to the confirmation that it is a

negative modulator of T-cell receptor activation adequately satisfies all tenets of the utility requirement and request that the utility rejection be withdrawn.

Although Applicants firmly believe that the Examiners utility rejection has been overcome, Applicants would like to refer the Examiner to the further teachings of McGlade et al (International Publication No. WO 02/42452, published May 30th, 2002; originally submitted with Applicants June 2nd, 2003 IDS). The teachings of McGlade et al are consistent with the teachings of Applicants specification in addition to the teachings of Pandey et al, Holland et al, and Loreto et al, and provide further post-filing publication corroborative evidence that the hSLAP-2 has utility, is in fact a new member of the SLAP family of adaptor proteins, and functions as a negative regulator of T-cell receptor activation. McGlade describes results obtained for a molecule that is 100% identical to hSLAP-2 which they refer to as MARS. McGlade teaches that hSLAP-2 inhibits T-cell receptor mediated NFAT activation (see page 35) which is consistent with its utility as a negative regulator of T-cell receptor activation since NFAT is a transcription factor that is activated by the T-cell receptor and results in transcriptional upregulation and expression of IL-2. McGlade further teaches that hSLAP-2 maps to chromosome 20 in a region that is frequently deleted in myeloproliferative disorders (see page 44), and in particular, premalignant hyperproliferative disorders of the myeloid cell population. McGlade also demonstrated that a cohort of patients with monoallelic deletions of chromosome 20q11 were found to have the hSLAP-2 specifically deleted. The latter finding directly associates the deletion of hSLAP-2 to the incidence of premalignant hyperproliferative disorders of the myeloid cell population. Applicants point out that the latter finding is directly corroborative with the teachings of Applicants specification relative to the utility of hSLAP-2 (see arguments presented *supra*, the arguments presented in Applicants August 18th, 2003 Reply, in addition to the utilities asserted in paragraphs 9, 12, 54, and 76 of Applicants specification). Applicants adamantly assert that hSLAP-2 adequately satisfies all tenets of the utility requirement and request that the utility rejection be withdrawn.

As Applicants stated in the August 18th, 2003 Reply, Applicants do not agree with the Examiners alleged application of Brenner v. Manson to the pending claims of the instant application. At issue in Brenner was whether a chemical process for synthesizing chemical compounds was patentable for an application that did not disclose any utility for the disclosed compounds (i.e., the patent application at issue in Brenner did not even describe the utility of the class of compounds that were orthologous to the claimed compounds at issue in the case either explicitly or through reference to a publication). Applicants assert that the instant patent application explicitly discloses the utility

of the hSLAP-2 polynucleotide and polypeptides, in addition to any modulators thereof, as originally filed. Thus, since the utility of hSLAP-2 is already disclosed in the specification, Brenner v. Manson cannot apply.

The Examiner also incorrectly alleges that paragraph 76 of Applicants specification states that "SPAP, not hSLAP-2, have been shown to be a negative regulator of intracellular signal transduction in several cell types including T-cells". Applicants point out that the term "SPAP" does not appear in paragraph 76, nor anywhere else within Applicants specification and that appropriate acknowledgement from the Examiner in the record is requested. The entire text of paragraph 76 is provided below for the Examiners reference.

> **[0076]** The present invention is based on the discovery of a novel full-length human Src homology 2-/ Src homology 3- (SH2/ SH3) domain-containing gene and its encoded protein, called hSLAP-2, which was determined by homology analysis to be a member of the SLAP family of adapter proteins. The gene and encoded product according to the present invention are called hSLAP-2 (human Src-Like Adapter Protein-2) due to its similarity with both human SLAP (hSLAP) and mouse SLAP (mSLAP) sequences. The SLAP proteins have been shown to be negative regulators of intracellular signal transduction in several cell types, including T-cells (see: Roche, S. et al., (1998) Src-like adaptor protein (Slap) is a negative regulator of mitogenesis. *Curr. Biol.* **8**:975-978; Tang, J. et al., (1999) SLAP, a dimeric adapter protein, plays a functional role in T cell receptor signaling. *Proc. Natl. Acad Sci. USA* **96**:9775-9780; and Sosinowski, T. et al., (2000) Src-like adaptor protein (SLAP) is a negative regulator of T cell receptor signaling. *J. Exp. Med.* **191**:463-474).

II. Rejections under 35 U.S.C. § 112, first paragraph

a. The Examiner has rejected Claims 21 to 25, 31, 33 to 37, and 41 to 44 under 35 U.S.C. § 112, first paragraph, alleging that the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility and that one skilled in the art clearly would not know how to use the claimed invention.

Applicants disagree. Applicants believe the Examiners allegations have been overcome in light of the arguments presented above, the arguments presented in the Applicants August 18th, 2003 Reply, the teachings of Applicants specification, in addition to the subsequent corroborative teachings of Holland et al, Pandey et al, Loreto et al, and McGlade et al. Since hSLAP-2 has a specific, substantial, and well established utility in the specification as originally filed, one skilled in the art clearly would know how to use the claimed invention. In addition, Applicants also assert that since the hSLAP-2 sequence, function, as well as its biological significance are disclosed in the specification as originally filed, Applicants specification provides the requisite teachings that a skilled artisan would require to use the claimed invention. Applicants request that the rejection under U.S.C. § 112, first paragraph be withdrawn for Claims 21 to 25, 31, 33 to 35, and 41 to 44. The rejection of Claims 36 and 37 is moot in consideration of Applicants cancellation of Claims 36 and 37.

III. Rejections under 35 U.S.C. § 112, first paragraph

a. The Examiner has rejected Claims 36 and 37 under 35 U.S.C. § 112, first paragraph, alleging that they contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. More particularly, the Examiner alleges "the specification does not reasonably provide enablement for an isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in Claims 36 and 37...Applicant discloses an isolated nucleic acid sequence of SEQ ID NO:1, encoding the full length hSLAP-2 polypeptide of SEQ ID NO:2 and complement thereof in the instant specification. Applicant has not taught how to make and/or use: any isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprising a heterologous nucleic acid sequence, claimed in Claims 36 and 37. The structural and functional characteristics of said nucleic acid molecules are not defined in the claim.

There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make the various nucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential and which sequences are nonessential-

There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the function of nucleic acid sequence or SEQ ID NO:1 and polypeptide encoded by the amino acid sequence of SEQ ID NO: 2. Moreover, there is insufficient guidance as to which "isolated polynucleotide comprising a heterologous polynucleotide", recited in the claims 36 and 37 would maintain the same function of the polypeptide encoded by amino acid sequence of SEQ ID NO: 1..."

Applicants disagree with the Examiners allegation and assert that one skilled in the art would clearly know how to make and use the claimed invention since the instant specification provides the polynucleotide and polypeptide sequences of hSLAP-2. Such sequences would be all that a skilled artisan would be need in order to make and use the invention based upon the level of skill in the art for cloning polynucleotides, for example. The Examiner alleges that the addition of a heterologous sequence or a heterologous sequence encoding a heterologous polypeptide to the hSLAP-2 coding sequence is somehow expected to alter the function of hSLAP-2. Applicants do not agree with this allegation, nor do Applicants understand the rational behind the allegation since fusion proteins are routinely created in the art that retain, and are expected to retain, the function of the host polypeptide. However, in the interest of facilitating prosecution and in recognition of the fact that the scope of Claim 21 encompasses any such heterologous sequences, in addition to any other sequences, that are appended to the sequences of Claim 21 as a consequence of the use of "comprising" language within the preamble of Claim 21, Applicants have cancelled Claims 36 and 37. Applicants believe the Examiners rejection of these Claims has been rendered moot in light of these cancellations.

IV. Rejections under 35 U.S.C. § 112, second paragraph

a. The Examiner has rejected Claims 36 and 37 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More particularly, the Examiner has rejected Claims 36 and 37 alleging that "Applicant is not in possession of: any isolated polynucleotide of claim 21 wherein said nucleotide sequence further comprises a heterologous nucleic acid sequence, claimed in

Claims 36 and 37...Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot

envision all the contemplated nucleic acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the

complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required...A description or a genus of nucleic acid sequences may be achieved by means of a recitation of a representative number of nucleic acid sequences, falling within the scope of the genus, or of a recitation of structural features common to the genus which features constitute a substantial portion of the genus".

Applicants disagree with the Examiners allegation and assert that one skilled in the art would clearly acknowledge that Applicants were in possession of the sequences embraced by Claims 36 and 37. However, in the interest of facilitating prosecution and in recognition of the fact that the scope of Claim 21 encompasses any such heterologous sequences, in addition to any other sequences, that are appended to the sequences of Claim 21 as a consequence of the use of "comprising" language within the preamble of Claim 21, Applicants have cancelled Claims 36 and 37. Applicants believe the Examiners rejection of these Claims has been rendered moot in light of these cancellations.

Applicants also assert that the Examiners rejections specific to genus claims (e.g., Fiers vs Revell; University of California v. Eli Lilly and Co.; and Vas-Cath Inc. v. Mahurkar) has also been rendered moot in consideration of Applicants amendments *supra*.

Applicants believe that all of the Examiners rejections and objections have been overcome and that all of the pending claims before the Examiner are in condition for allowance. An early Office Action to that effect is, therefore, earnestly solicited.

If any fee is due in connection herewith not already accounted for, please charge such fee to Deposit Account No. 19-3880 of the undersigned. Furthermore, if any extension of time not already accounted for is required, such extension is hereby petitioned for, and it is requested that any fee due for said extension be charged to the above-stated Deposit Account.

Respectfully submitted,

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